MMTV and Its Interaction with the Immune System

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Mouse mammary tumor virus (MMTV) is a retrovirus that causes mammary tumors in mice by inserting next to cellular oncogenes and activating their expression. MMTV is both inherited through the germ line and passed as an infection virus from mothers to offspring through milk. We are investigating the tissue-specific expression of MMTV *in vivo* and have found that the virus encodes regulatory regions that allow it to be efficiently expressed in mammory gland and passed through milk. We also discovered that the virus is expressed in several tissues besides mammory gland, most notably, in lymphoid organs. These results are important to understanding normal gene expression and how this virus has adapted to efficient use of its host for propagation.

The finding that MMTV is expressed in lymphoid tissue is of great interest for several reasons. The first is that there are variants of MMTV that cause T cell lymphomas. These variants have deletions in the transcriptional regulatory regions found in the long terminal repeats (LTRs), which may result in increased expression in lymphoid cells. Moreover, there is a protein encoded in the MMTV LTR that belongs to the class of antigens termed "superantigens" (Sag); part of the coding potential for this protein is deleted in the T-lymphoma-associated MMTV variants. Antigen presenting cells (APCs), such as B cells, present Sag proteins to T cells and cause the proliferation of T cells bearing specific Vβ chains of the T cell receptor. We have shown that MMTV infects mice because the viral Sag protein in infected APCs stimulates T cells to divide and that this stimulation is a requisite step in for milk-borne infection. Conversely, mice that delete Sag-cognate T cells during shaping of the immune repertoire because they contain endogenous MMTVs are immune to infection; this is because they lack T cells capable of being stimulated by the Sag. These results may have implications for human viral infection, since it has recently been shown that rabies virus and perhaps other viruses encode superantigens. Thus, one could envision an antiviral therapy that involves deletion of the T cells targets of the superantigens.

Source: https://www.industrydocuments.ucsf.edu/docs/yfdb0000